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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/553,993	04/20/2000	Kevin Gunderson	A-69235/DJB/RMS/DCF	5906

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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1655	14

DATE MAILED: 11/27/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/553,993	GUNDERSON ET AL.	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 19 November 2001 in Paper No. 13 in which claims 1, 2, 10 and 14 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 9 dated 18 May 2001 under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments and Applicant's remarks regarding Claim 6. The previous rejections under 35 U.S.C. 103(a) are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

Currently claims 1-14 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al. (U.S. Patent No. 6,027,889, filed 28 May 1997) in view of Walt et al. (U.S. Patent No. 6,023,540, filed 14 may 1997).

Regarding Claim 1, Barany et al. teach a method of detecting a target nucleic acid sequence, said method comprising: attaching a first adapter nucleic acid to a first target nucleic acid sequence to form a modified first target nucleic acid sequence; contacting said modified first target nucleic acid with an array comprising: a substrate with a patterned surface comprising discrete sites and at least a first sub-population on said substrate

comprising a first capture probe, such that said first capture probe and said modified first target nucleic acid sequence form a hybridization complex; and detecting the presence of said modified first target nucleic acid sequence (Column 26, line 37-Column 27, line 19 and Claim 13). The extra method steps of Barany et al. are encompassed by the open claim language "comprising" of the instant claims. Barany et al. do not teach the method wherein the array further comprises a population of microspheres which comprise the first sub-population comprising a first capture probe; wherein said microspheres are distributed on said surface. However, Walt et al. teach a similar method for detecting a target nucleic acid sequence comprising: contacting said first target nucleic acid sequence with an array comprising: a substrate with a patterned surface comprising discrete sites; and a population of microspheres comprising at least a first sub-population comprising a first capture probe such that said first capture probe and said first target nucleic acid sequence form a hybridization complex, wherein said microspheres are distributed on said surface (Column 4, lines 4-14); and detecting the presence of said first target nucleic acid sequence (Column 10, lines 4-41) wherein microspheres comprising different capture probes are mixed but individually detected and identified allowing for individual identification of thousands of captured target sequences using an apparatus which is easy to use and manufacture (Column 3, lines 17-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on the array at discrete site and wherein the microspheres comprise the capture probes for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 2, Barany et al. teach the method further comprising: attaching a second adapter nucleic acid to a second target nucleic acid sequence to form a modified second target nucleic acid sequence; contacting said modified second target nucleic acid sequence with

said array wherein said array comprises at least a second sub-population comprising a second capture probe such that said second capture probe and said modified second target nucleic acid sequence form a hybridization complex; and detecting the presence of said modified second target nucleic acid sequence (Column 26, lines 55-67) but they do not teach a population of microspheres. However, Walt et al. teach the similar method further comprising a second target nucleic acid sequence and contacting said second target nucleic acid sequence with said array wherein said population of microspheres comprises at least a second sub-population comprising a second capture probe such that said second capture probe and said first target nucleic acid sequence form a hybridization complex, wherein said microspheres are distributed on said surface (Column 4, lines 4-14); and detecting the presence of said second target nucleic acid sequence (Column 10, lines 4-41) wherein microspheres comprising different capture probes are mixed but individually detected and identified allowing for individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use (Column 3, lines 17-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on the array at discrete site and wherein the microspheres comprise the capture probes for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 3, Barany et al. teach the method wherein said attaching is by an amplification reaction (Column 9, line 61-Column 10, line 23).

Regarding Claim 4, Barany et al. teach the method wherein said amplification reaction is the polymerase chain reaction (Column 9, line 61-Column 10, line 23).

Regarding Claim 5, Barany et al. teach the method wherein said amplification reaction is the oligonucleotide ligation amplification reaction (Column 9, lines 17-60).

Regarding Claim 6, Barany et al. teach the method wherein said attaching is by chemical synthesis i.e. the oligonucleotides primers comprising the adapters are synthesized using phosphoramidite chemistry (Column 46, lines 25-50).

Regarding Claim 7, Barany et al. teach the method wherein said modified target nucleic acid sequence comprises a label (Column 9, lines 61-67).

Regarding Claim 8, Barany et al. teach the method wherein said label is a fluorescent label (Column 46, lines 24-50).

Regarding Claim 9, Barany et al. teach the method wherein said adapter nucleic acid is labeled i.e. 5' end of the adapter primer is labeled (Column 46, lines 24-50).

Regarding Claim 10, Barany et al. teach the method wherein said target nucleic acid sequence is labeled prior to attaching (Column 46, lines 24-50).

Regarding Claim 11, Barany et al. teach a method of detecting a target nucleic acid sequence, said method comprising: attaching a first adapter nucleic acid to a first target nucleic acid sequence to form a modified first target nucleic acid sequence; contacting said modified first target nucleic acid with an array comprising: a substrate with a patterned surface comprising discrete sites comprising at least a first sub-population comprising a first capture probe, such that said first capture probe and said modified first target nucleic acid sequence form a hybridization complex; and detecting the presence of said modified first target nucleic acid sequence (Column 18, line 22-Column 19, line 22). The extra method steps of Barany et al. are encompassed by the open claim language "comprising" of the instant claims. Barany et al. do not teach the method wherein the array further comprises a population of microspheres which comprise the first sub-population comprising a first capture probe; wherein said microspheres are distributed on said surface. However, Walt et al. teach a similar method for detecting a target nucleic acid sequence comprising: contacting said first target nucleic acid sequence with an array comprising: a substrate with a patterned surface comprising discrete sites; and a population of microspheres comprising at least a first sub-

population comprising a first capture probe such that said first capture probe and said first target nucleic acid sequence form a hybridization complex, wherein said microspheres are distributed on said surface (Column 4, lines 4-14); and detecting the presence of said first target nucleic acid sequence (Column 10, lines 4-41) wherein microspheres comprising different capture probes are mixed but individually detected and identified allowing for individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use (Column 3, lines 17-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on the array at discrete site and wherein the microspheres comprise the capture probes for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 12, Barany et al. teach the substrate is an array (Column 27, lines 10-15) but they do not teach the array is a fiber optic bundle. However, Walt et al. teach the similar method wherein the substrate is a fiber optic bundle (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on a fiber optic bindle substrate for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 13, Barany et al. teach said substrate comprises discrete sites (Column 27, lines 10-15) but they do not teach said discrete sites comprise wells. However, Walt et al. teach the similar method wherein said discrete sites comprise wells (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the discrete sites on the substrate of Barany et al. to provide

microspheres distributed on a substrate at the discrete sites and wherein each discrete site comprises a well for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 14, Barany et al. teach a method of detecting a target nucleic acid sequence comprising: hybridizing a first primer to a first portion of a target sequence wherein said first primer further comprises an adapter sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primers to form a modified primer; contacting said adapter sequence of said modified primer with an array comprising: a substrate with a surface comprising discrete sites comprising at least a first sub-population comprising a first capture probe, such that said first capture probe and said modified first target nucleic acid sequence form a hybridization complex; and detecting the presence of said modified first target nucleic acid sequence (Column 26, line 37-Column 27, line 19 and Claim 13). The extra method steps of Barany et al. are encompassed by the open claim language "comprising" of the instant claims. Barany et al. do not teach the method wherein the array further comprises a population of microspheres comprising the at least first sub-population wherein said microspheres are distributed on said surface. However, Walt et al. teach a similar method for detecting a target nucleic acid sequence comprising: contacting said first target nucleic acid sequence with an array comprising: a substrate with a patterned surface comprising discrete sites; and a population of microspheres comprising at least a first sub-population comprising a first capture probe such that said first capture probe and said first target nucleic acid sequence form a hybridization complex, wherein said microspheres are distributed on said surface (Column 4, lines 4-14); and detecting the presence of said first target nucleic acid sequence (Column 10, lines 4-41) wherein microspheres comprising different capture probes are mixed but individually detected and identified allowing for individual identification of thousands of captured target sequences using an apparatus which

is easy to manufacture and use (Column 3, lines 17-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on the array at discrete site and wherein the microspheres comprise the capture probes for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Response to Arguments

4. Applicant argues that there is no expected benefit to modify the arrays of Barany et al. with the teaching of Walt et al. because the arrays of Barany et al. are already high density arrays. The argument is not found persuasive because Walt et al. clearly teaching motivation for modifying the high density arrays of Barany et al. with their arrays of microspheres i.e. the arrayed microspheres prove an "extremely uniform" signal and the signals can be analyzed using commercially available software whereby signals can be detected automatically within seconds (Column 4, lines 15-28). Therefore, one skilled in the art would have been motivated to modify the high density array of Barany et al. with the arrayed microspheres as taught by Walt et al. for the benefits taught by Walt et al. i.e. speed and accuracy of detection (Column 4, lines 15-28).

Applicant argues that the teachings of Walt et al. would change the principle of the array of Barany et al. and therefore, the combination of the two references is not allowed by the MPEP. The argument has been considered but is not found persuasive because the principle operation of the Barany et al. reference is the detection of nucleic acid sequences wherein the sequences are immobilized in an array and detected (Abstract). Additionally, the principle operation of Walt et al. is detection of chemical functionalities (e.g. nucleic acids) wherein the functionalities are immobilized in an array and detected (Abstract). Therefore, both Barany et al. and Walt et al. share principle operations. It is noted that the resiliency Vs rigidity cited by Applicant (*In re Ratti* 270 F.2d 810 (CCPA 1959)) is irrelevant with regard to the instant rejection because principle operation of Barany et al. and Walt et al. is the same i.e. detection of nucleic acid sequences wherein the sequences are immobilized in an array and detected.

Applicant further argues that Barany et al. and Walt et al. alone or in combination to not motivate one of skill in the art to combine the teachings to arrive at the instantly claimed invention and therefore the instantly claimed invention is nonobvious. The argument is not found persuasive because the courts have stated "It is prima facie obvious to combine two

compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (see MPEP, 2144.06). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the substrate for immobilizing nucleic acids of Barany et al. with the substrate for immobilizing nucleic acids of Walt et al. based on their equivalent purpose in the prior art (i.e. immobilization of nucleic acids) because the idea of combining them logically flows from the teachings in the prior art. Therefore, one skilled in the art would have been motivated to combine the teachings and to immobilize the nucleic acids of Barany et al. in an array of microspheres as taught by Walt et al. of for the benefits taught by Walt et al. i.e. speed and accuracy of detection (Column 4, lines 15-28).

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 and 15-16 of copending Application No. 09/535,854. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims, drawn to a method of detecting a target nucleic acid, are a genus of the '854 claims which are drawn to a method of determining the identification of a nucleotide at a detection position in a target sequence and a genus is obvious over the species. Therefore, the instant claims are obvious over the '854 claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 1-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-41 of copending Application No. 09/425,633. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims, drawn to a method of detecting a target nucleic acid, are a species of the '633 claims which are drawn to a method wherein both sets of claims comprise similar method steps and therefore the instant claims are obvious over the '633 claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 1-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 09/513,362. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims, drawn to a method of detecting a target nucleic acid, are a genus of the '362 claims which are drawn to a method of sequencing a target sequence wherein both sets of claims comprise similar method steps. The genus is obvious over the species and therefore, the instant claims are obvious over the '362 claims.

9. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
November 27, 2001